

**REMARKS/ARGUMENTS**

Claims 13-26 are pending in the application.

Claims 21-23 are allowed.

Claims 1-12 were cancelled in the last response.

Claims 13-20 and 24-26 stand rejected.

Claims 13, 24, 25 and 26 have now been amended to define the type of bonding occurring on the surface of the carrier. The type of bonding on the carrier is defined as covalent and electrostatic.

Applicant is grateful for the interview granted by Examiner Forman on 16 March, 2004. At the interview, the Examiner stated that the claim reads on hydrogen bonds formed during hybridization. The currently amended independent claims now define the type of bonding on the surface and accordingly distinguishes over hydrogen bonds formed during hybridization. However, although Applicant does not want to be limited to theory, Applicant believes that this limitations do not preclude other types of bonding that may occur since the surface of Applicant's carrier does not contain complementary nucleic acids necessary for hybridization.

The use of the language covalently or electrostatically is fully supported by the examples and specification.

**THE REJECTION UNDER 35 U.S.C. § 102(b)**

The rejection of Claims 13-15, 17 and 24-26 under 35 U.S.C. § 102 (b) as being anticipated by Cronin et al (U.S. Patent No.6,045,996, issued 4 April 2000) is respectfully traversed.

In issuing the outstanding office action, The Examiners' states the following:

"With respect to claim 13, Cronin et al disclose a process for binding nucleic acids to a carrier wherein the nucleic acids are dissolved in a solvent containing at least one betaine, applying the nucleic acid-betaine solution to the carrier whereby the nucleic acids are bound to the carrier i.e. via hybridization to a probe immobilized on the carrier (Column 10, line 48-Column 11, line 20).

Regarding claim 14, Cronin et al. disclose the process wherein the betaine is trimethylmammoium acetate (Column 4, lines 22-31), and regarding Claim 3, Cronin et al. disclose the process wherein the betaine is present at a concentration of 8mM to 6.5M (Column 4, lines 3-31 and Column 5, lines 11-12).

Regarding Claim 15, Cronin et al. disclose the use of betaines as additives for solvents in which nucleic acids are dissolved in order to bind them to a carrier i.e. via hybridization to probe immobilized on the carrier (Column 10, line 48-Column 11, line 20).

Regarding Claim 17, Cronin et al. disclose the process wherein the carrier is made of glass (col. 10, lines 17-19).

Regarding claim 24-26 Cronin et al disclose a process for binding nucleic acids to a carrier comprising adding a betaine to a solution of nucleic acids and subsequently applying the solution to the carrier whereby the nucleic acids are bound to the carrier i.e. via hybridization to a probe immobilized on the carrier (Column 10, line 48-Column 11, line 20).

According to the present invention as now defined in currently amended claims 13, and 24-26, the bonding occurs via covalent or electrostatic bonds and accordingly the rejection under Cronin et al. is now moot.

Reiterating our prior arguments, Cronin et al. describes in the abstract and specification *"methods of performing nucleic acid hybridization assays on high-density substrate-bound oligonucleotide arrays involving including in the hybridization mixture and isostabilizing agent, a denaturing agent or a renaturation accerlerant"*. According to column 3, lines 32 to 37 of Cronin et al., *"a hybridization mixture containing the target and an isostabilizing agent..... is brought into contact with the probes of the array and incubated at a temperature and for a time appropriate to allow hybridization between the target and any complementary probes"*. The terms "probe" and "target" are defined in column 2, lines 58 to column 8, lines 8 of Cronin et al. The "probe" is *"a surface-*

*immobilized oligonucleotide that can be recognized by a particular target*". This means that the "probes" are the nucleic acids, which are bound onto the surface of a DNA microarray. The "target" is defined in Cronin et al, as " *a nucleic acid molecule that has an affinity for a given probe*". According to Cronin et al., "*betaines*" are used as *isostabilizing agents*", see column 4, lines 7 to 9.

In other words, Cronin et al. teaches that the nucleic acids to be investigated and a betaine are contacted with a microarray (a support having immobilized on its surface a nucleic acid complementary to the nucleic acid to be investigated). The nucleic acid to be investigated is hybridized to the nucleic acid of the array. Furthermore, Cronin et al. teaches the use of arrays in hybridizing the target nucleic acid to it with the help of a betaine but not the production of arrays or the binding of the nucleic acid to a carrier or to the surface of the microarray.

In contradistinction, the instant invention is directed to the spotting and binding of nucleic acids onto a carrier by using betaines. In the spotting and binding process of the invention, probes are immobilized onto the carrier, i.e. microarrays are produced. The spotting and binding process of nucleic acids to a carrier as claimed in the instant invention is very different from the hybridization method described in Cronin, et al. With the spotting and binding process of the invention microarrays are produced. In the hybridization method taught in Cronin, et al., the microarray is used to perform such hybridizations. Accordingly, the present invention as now defined with the currently amended claims 13, and 24-26, is novel and also based on an inventive step and

distinguishable over of Cronin, et al.

Claims 13-15, 17, 24 and 26 stands rejected under 35 U.S.C. § 102 (b) as being anticipated by Koster et al (U.S. Patent No. 5,547,835).

For the reasons set forth above and the introduction of the language “covalently and electrostatically” binding the nucleic acids, it is believed that the rejection under Koster is also now moot.

**THE REJECTION UNDER 35 U.S.C. § 103(a)**

The rejection of claims 16, and 18-20 under 35 U.S.C. 103 (a) as being unpatentable over Koster (U.S. Patent No. 5,547,835) in view of DeRisi et al (Science, 24, 278: 680-686 (1997)) is courteously traversed.

Neither Koster alone or Koster in view of DeRisi et al. anticipate the subject matter of the instant invention as none of them have motivation to covalently or electrostatically bind nucleic acids to a carrier. Applicant has reviewed the Koster reference and does not find a teaching of covalently or electrostatically binding a nucleic acid to a carrier. Same arguments apply to the rejection of claims 18-20.

Thus, the present invention as now currently claimed is also novel and patentable Koster in view of DeRisi et al.


It is respectfully requested that the rejections under 35 U.S.C. § 103(a) be withdrawn.

**NOTICE TO COMPLY WITH NUCLEIC ACID SEQUENCE RULES**

Regarding the notice to comply with nucleic acid sequence rules, it is respectfully requested that the Examiner review the specification carefully as Applicant believes that the instant case does not require a sequence listing.

In view of the above amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejections and objections are requested. The Examiner is invited to contact the undersigned at 703-418-2777 if she feels that further discussion may facilitate the resolution of any outstanding issues. An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

  
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Isaac Angres  
Reg. No. 29,765

Date: May 12, 2004  
2001 Jefferson Davis Highway--Suite 301  
Arlington, VA 22202  
(703) 418-2777  
Ref: 22012.PUSa